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# Revisiting density dependence in human schistosomiasis using sibship reconstruction

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### What is the research?

Schistosomiasis is a devastating neglected tropical disease caused by trematode parasites of the genus Schistosoma. Although earmarked for control and elimination by the World Health Organization, schistosomiasis remains a major public health concern, endemic in 54 countries and affecting approximately 240 million people worldwide. Moreover, many fundamental aspects of schistosome population biology remain unresolved, impeding the design, optimisation and evaluation of intervention strategies targeting control and elimination. A key unknown is whether and to what extent schistosome populations are regulated by density-dependent population processes. In dioecious helminth infections, density-dependent fecundity describes the reduction in egg production by female worms in high worm burden within-host environments. For human schistosomiasis, unlike some intestinal worms, investigating density-dependent fecundity is hampered by the inaccessibility of adult worms within hosts, due to the intravascular location of the parasite. Current understanding of this fundamental population process is limited to data collected from two autopsy studies conducted over 40 years ago, with subsequent analyses having reached conflicting conclusions on the operation of densitydependent egg production.

Sibship reconstruction is a branch of parentage analysis which can be used to estimate the number of parents/ adult worms in individual human hosts from molecular data derived from the accessible transmission stages/offspring of schistosomes. In combination with egg count data, this provides a novel means to identify density-dependent fecundity, albeit using robust statistical methodologies

to account for the bias and uncertainty of worm burden estimates which depend on the number of offspring sampled. We illustrate this approach using a recent multiplexed microsatellite dataset derived from *Schistosoma* spp. miracidia hatched from infected samples of children undergoing preventive chemotherapy in Tanzania.

> Relaxation of the density-dependent fecundity of *S. mansoni* parasites within a host after treatment with praziquantel. Photo credit: Joanne Webster

#### Why is this research necessary?

Density dependencies enhance the resilience of parasite populations to interventions, a critical consideration when designing intervention strategies and interpreting data on the effectiveness of control. In particular, in schistosomiasis – and indeed many other helminthiases with inaccessible adult parasite stages – infection intensity is inferred from indirect measures of egg output, a proxy for the number of infecting adult female parasites. Whether egg production is regulated in a density-dependent manner is key to interpreting routine egg count data and has important ramifications for predicting or modelling the response of schistosome populations to perturbation by intervention.

## What is the research impact?

We estimated a non-proportional relationship between *Schistosoma* spp. egg counts and inferred numbers of female worms, indicating that egg production is suppressed in individuals with higher worm burdens, suggesting density-dependent fecundity. Resolving this fundamental question will have multiple public health implications, including for policy decisions informed by the modelled transmission dynamics of schistosomes during intervention and for the interpretation of egg count data collected during monitoring and evaluation activities. Therefore, future work will focus on the validation of this approach by comparison between direct and indirect methods of estimating worm burdens in infected animal hosts and re-evaluating density dependence using paired molecular and parasitological data.



